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SECOND LEES AND RAPER MEMORIAL LECTURE.

THE

EFFECT OF ALCOHOL

UPON THE

HUMAN BRAIN:

A LECTURE BY

SIR VICTOR HORSLEY, M.B., F.R.C.S., F.R.S.,

DELIVERED IN

St. James' Hall, London,

—— ON ——

FRIDAY, APRIL 27th, 1900,

UNDER THE PRESIDENCY OF

AUGUSTINE BIRRELL, K.C., M.P.

THE LEES & RAPER MEMORIAL LECTURESHIP.

The Lectures deal with the varied aspects of the Temperance Reform, and were designed to perpetuate the memory and continue the work of the late FREDERIC RICHARD LEES, Ph.D., F.S.A., and JAMES HAYES RAPER, both of whom were zealously engaged for over Sixty years in many departments of Temperance and Social Reform — Dr. Lees being a great Philosopher and Teacher, and Mr. Raper one of the foremost Orators of his time.

The Effect of Alcohol

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Sir VICTOR HORSLEY, M.B., F.R.C.S., F.R.S.

——— ——

On the occasion of a lecture such as the present, which is designed to perpetuate the memories of two advocates of the Temperance cause, Dr. Lees and Mr. Raper, it appears to me almost a duty to present to you the existing state of scientific knowledge on the Temperance question, and I therefore propose to summarise the work that has been done most recently on the effect of taking into the body, not of large quantities of alcohol (for we all recognise that as injurious), but of those small quantities which are ordinarily used at meal times and are spoken of as dietetic. Looked at from a purely scientific standpoint, the question of alcohol and its effects is one of fact alone, however much each one of us may be personally moved by the tragedies and poverty involved in it, and therefore though all scientific subjects have a socio-political bearing, and none more markedly so than that of alcohol, I shall present the question, I hope, without bias and solely from the basis of scientific evidence.

The special branch of the discussion which I wish to bring before you this evening is, as I have said, that of the effect of small quantities of alcohol upon the brain, the governing body of the organism. Now, although alcohol has been used as an article of diet for thousands of years the injurious effect of even relatively large quantities has only comparatively recently become thoroughly understood from a medical point of view. In fact, so completely are we still at the threshold of the subject, that it is only within the last twenty years that the graver effects of large doses has in many special respects been elucidated. Though, however, this fact is patent to all scientific workers, the effects of excessive quantities of alcohol are frequently spoken of with confidence by those who have given (at the best) but a superficial attention to the subject, and are not equipped with the special knowledge necessary to diagnose the evils which it engenders.

Alcohol the Unsuspected Cause of Certain Forms of Paralysis.

Thus, while there are forms of paralysis which are now well recognised by the medical profession to be the direct effect of alcohol poisoning, the individuals affected are never considered by their friends to be drunk, nor are they ever in the popular sense intoxicated, *i.e.*, rendered partly unconscious, and thus the origin of the disease is not ascribed to its true cause.

Turning now from these deep-seated and chronic alcoholic affections to the consideration of the more immediate effects of the drug, it may possibly be unknown to some of those present that all drugs have a selective action, that is, that they act on the various parts of our structure by means of a chemical affinity, and it follows therefore that as these parts differ from one another so also do the effects produced upon them. In fact, as Professor Ehrlich has pointed out, the action of any drug is merely a question of chemical affinity, under which some organs or even parts of organs are affected and others are spared.

The Action of Alcohol on the Peripheral Nerves.

This is particularly observable in the case of alcohol, which acts especially on the peripheral nerves, *i.e.*, on the nerves running in the limbs and the extremities, and thus it is that when alcohol is taken in quantities not sufficient to produce drunkenness, but enough to justify the term "soaking," we see that these nerves in the extremities become paralysed.

It is to be noted that though this condition must have been observed for thousands of years, it is only within the last forty that its signification has been understood.

We must now familiarise ourselves with the various elements of the nervous system which investigation has shown to be the commonest points of attack.

The contents of the skull consist of a large brain or cerebrum and a small brain or cerebellum, both of these being connected by nerve fibres in the spinal cord with the nerves in the limbs, with the sensory nerve endings in the skin, and with the muscles.

The relations of all these parts is strikingly exhibited in one of Professor Fraser's photographs (fig. 1) of the head and neck in which the outer part of the skull and the soft parts have been removed, shewing the large and the small brain with the spinal cord leading downwards from thence. From the spinal cord nerves may be seen running out into the neck and thence into the upper limb.

The next photograph is a representation of a plaster cast (fig. 2) of a dissection by Professor Cunningham, in which is shown very clearly the convoluted surface of the large brain. Your attention must first be directed to the fact that the two principal grooves, the fissure of
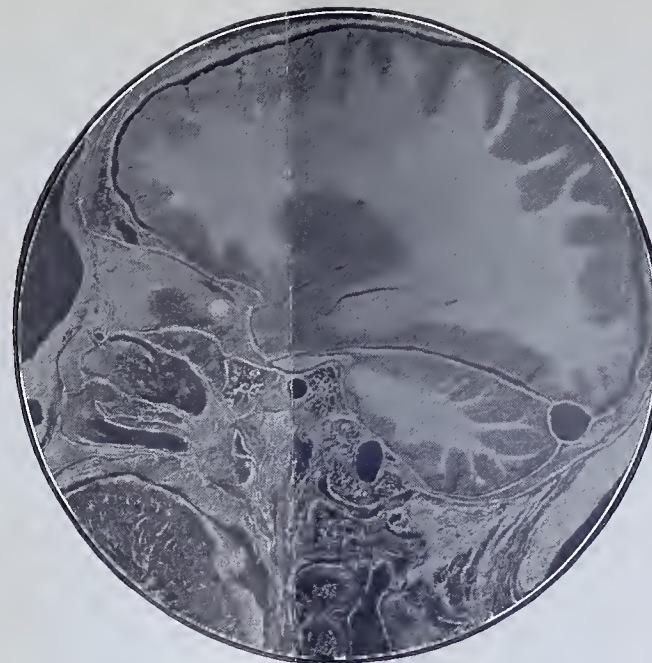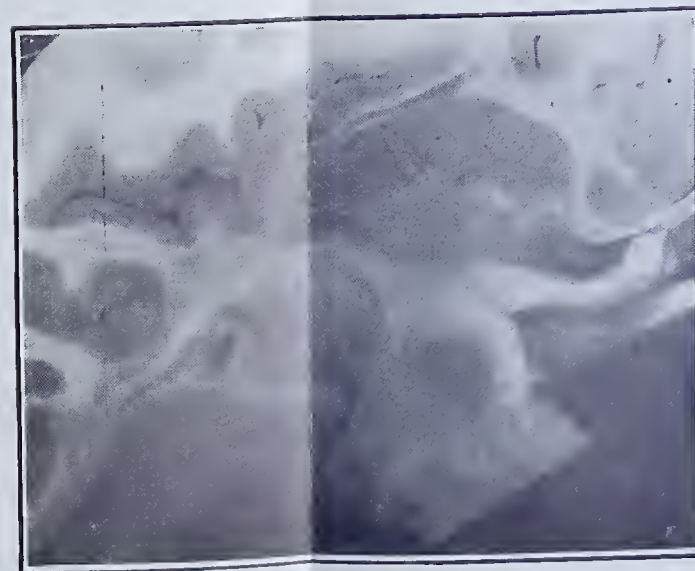
Fig. 1.
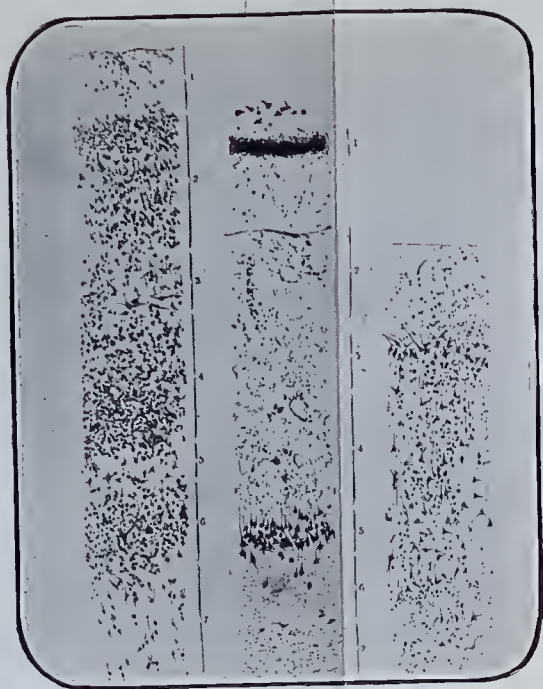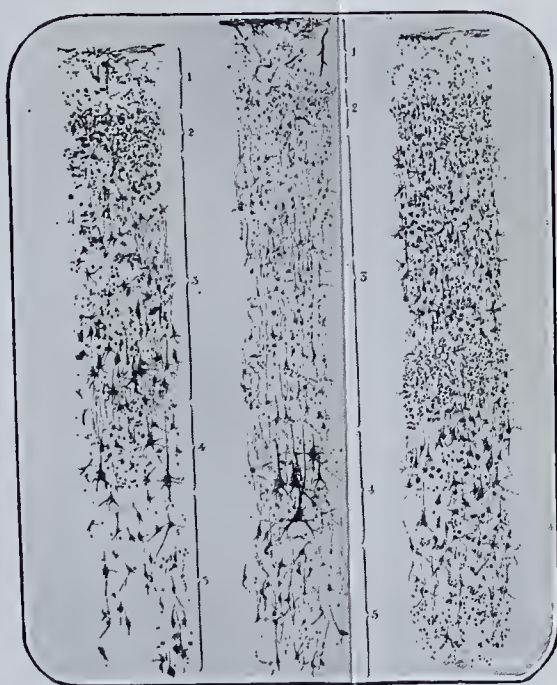

Fig. 2.

Fig. 3.

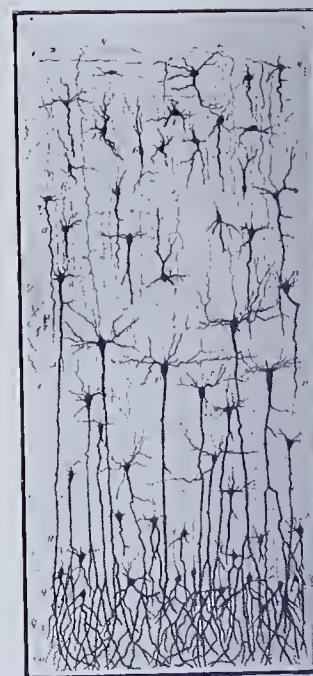Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Rolando and the fissure of Sylvius, separating these convolutions are no arbitrary lines of division, but are constant and of great importance in our study of the topography of the brain.

All the frontal lobe is a terra incognita, but in the parietal lobe are the stations whence the orders are issued to the muscles for the performance of voluntary acts. The hinder or occipital part of the hemisphere, especially in its inner aspect, is for visual perception, the temporal region for hearing, and the tips and the inner aspect of the temporosphenoidal lobe is for the perception of taste and smell respectively.

If we make a vertical section through the brain parallel to the mesial plane of the body, it is obvious that the convoluted surface consists of grey matter, and that there is grey matter also in the depth of the brain (see fig. 3). Issuing from the grey surface of the brain are innumerable bundles of white fibres making up the white substance continuous with the spinal cord.

The cerebellum or small brain has the same general structure, *i.e.,* grey matter on the surface and white fibres in its interior.

Fig. 4 is a section of a part of a chimpanzee's brain, which, of course, is exactly like ours, demonstrating rather better the grey convoluted surface and the white fibres passing to the spinal cord. Below is the optic nerve—(the seeing nerve), and further, the optic fibres running back to the hemisphere of the brain. In every voluntary act, for example in touching any object, we see what we want to touch through this little part of the brain.

The Structure of the Cortex of the Brain.

The next step is the discussion of the structure of this cortex or surface of the brain which is formed in convolutions.

If we examine a vertical section of the cortex we see that it is made up of layers. This section (fig. 5) represents the whole depth of the grey substance of the occipital lobe, the seat of the visual centre. It is made up of different layers of small bodies which we call nerve corpuscles, which get larger as we go deeper. It is also made up of fibres coming to and going from these bodies, which we shall discuss further directly.

These (fig. 6) are sections or thin slices of portions of grey matter from parts of the brain, showing structural differences according to the different functions served.

This (fig. 7) is from the region of the centres for muscular movements, being a section of the parietal cortex. It is composed of small cells in the upper layers and then very large ones in the deeper, which are the large out-going stations from which the impulses run down the spinal cord and out through the nerves to the muscles.

This is a section from the auditory part of the brain.

We must consider now the nature of these little cells rather more closely.

Thus the visual centre (occipital lobe) has, as you will see from Dr. Bevan Lewis's specimen (fig. 5), a different structure from the parietal region, in which are grouped the centres for different movements.

Roughly speaking, each nerve centre consists of small nerve corpuscles and large nerve corpuscles, and in those parts of the brain which have to do with the perception of special senses, sight, hearing, etc., the small corpuscles predominate, whereas in that part of the brain which has to do with giving out the orders to the muscles by the way of voluntary movement the large nerve corpuscles are the most characteristic feature.

This next section illustrates (by a different method of staining, invented by Professor Golgi relatively recently) these nerve cells with their remarkable processes.

This large cell gives out a fibre which is in connection with the white substance of the hemisphere. Here, however, is a process from the cell which branches out, but does not come into physical conjunction with its fellows on the surface of the brain.

Here is one little cell (fig. 8) very highly magnified and stained with methylene blue. This section brings out the fact that the cell substance is made up of a very delicate reticulum or network with deeply staining parts, which have received the name of granules. These are arranged in different kinds of nerve cells in a characteristic way. Then there is also, as in every cell of the body, a nucleus which is a kind of little sac containing in a delicate net-work a nucleolus which often has again a second nucleolus within it. The position of the nucleus is important, it should occupy about the middle of the cell.

I will show you one more drawing of a nerve cell, merely to illustrate the complicated way in which the nerve fibres come into contact with the cells. Here is a section (fig. 9) where the fibres are in connection with a cell, one fibre is leaving the substance, and another is here breaking up into a net-work around it.

The surface of the great brain consists of a mass of nerve centres, each composed of a number of such small nerve corpuscles and their branches (fig. 10). The precise work of these delicate structures is not finally decided, but they have a very definite arrangement, according to the function of the part of the brain which they compose.

So far, then, we have considered the structure of the highest part of the brain, the structure of the cortex or grey matter on the surface which has to do with our thinking, which subserves the reception of sensations and which gives out orders for the performance of our acts, but we have to-night to discuss a much larger question, on which we cannot speak with such positiveness as I have done respecting the mere reception of sensory impressions and the issuing of orders to the
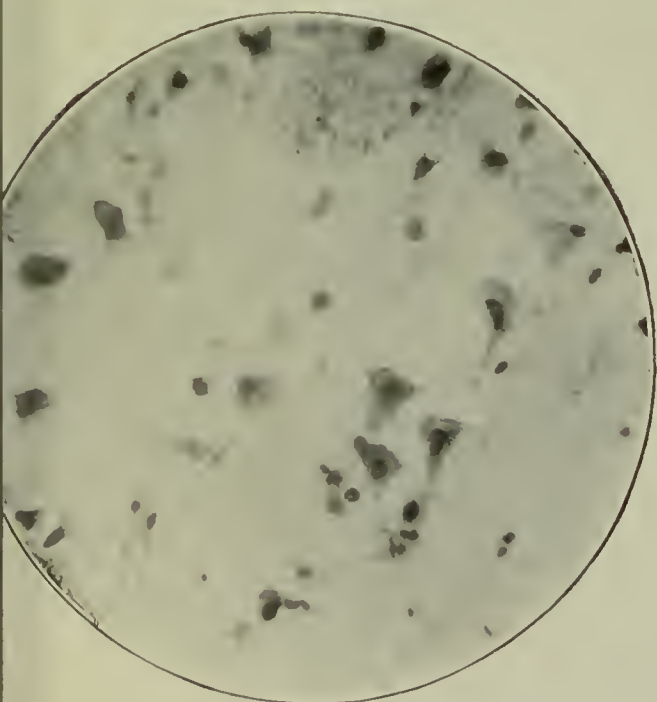
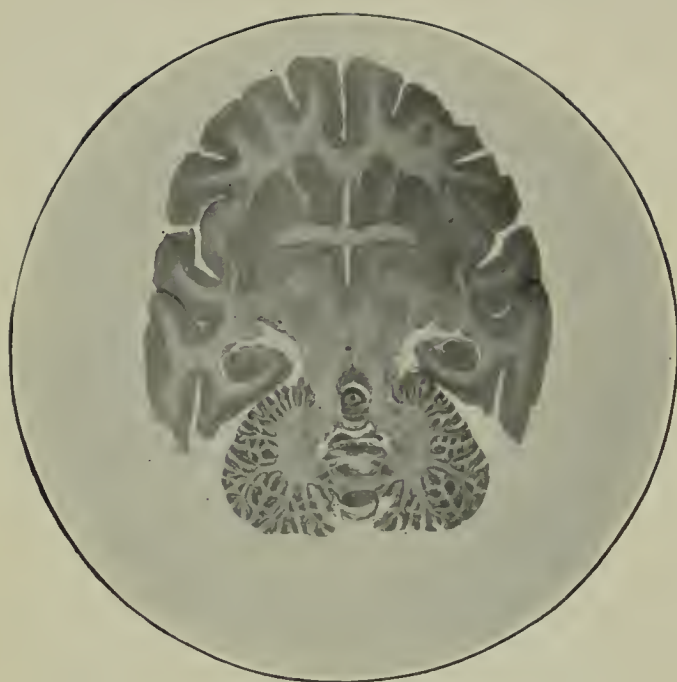Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

muscles. We have, in fact, to consider what part of this grey matter or cortex it is which subserves the operations of the mind. Our ideas are recorded in this grey matter, but where? and what part of the cortex is occupied in even such a simple form of ideation, as the adding up of a small column of figures, or the recognition of an object? You must take it from me that evidence goes to show that it is these smaller cells you have seen which are the mechanism underlying the operations of the mind, that in these smaller cells are recorded the memories of things we have learnt, and that therefore they are in a state of functional activity at the time when we are thinking something. I should like to draw your attention to the fact that there is no evidence to show that the frontal lobes, which are usually credited with being more or less the chief seat of mentation, are alone occupied when we are thinking of something seriously, in fact there is other evidence to show that when our brain is fully occupied practically the whole cortex is in a state of activity. We see that in numerous ways. If one watches people who are thinking very intently and whose nervous systems are in some state of excitement, we observe their limbs to move and other phenomena to present themselves, showing that every part of the cortex is in a condition of disturbance. We now know that the memories of movement constitute a most important part of what we call a voluntary act, quite as important as the outgoing impulse causing the movement of the muscle.

The Structure of the Cerebellum.

I have now shown the parts of the brain which we know to be affected by alcohol in small quantities, with the exception of one part, to which I have now to draw your attention. The portion of the nervous system in question is called the cerebellum, or small brain. This (fig. 11) is a horizontal section taken on the flat through the hemispheres of a monkey. Here we have the great brain and here the small brain or cerebellum, and you can readily see the difference in structure. I only want to remind you that this little brain must be in a state of activity when the large brain is, and especially when this central part of the cortex of the brain is performing a voluntary muscular act, because as we shall see in the correct performance of such acts the cerebellum is an organ which is of the greatest importance.

Inasmuch, therefore, as one of the effects of alcohol is to disorganise the accurate execution of muscular action, we must look for some effect of the drug on the cerebellum as well as on the great brain.

To appreciate the effects of small quantities of alcohol on the central nervous system we have to investigate the subject under the headings: First, the effect on ideation, or on the higher psychical functions of the brain. Secondly, the effect on the nervous apparatus for voluntary action, or in other words the effect on the centres in the region of the parietal lobe for voluntary movements. And thirdly, the effect on the cerebellar apparatus for the regulation of movement

and equilibration, or to state it more precisely the effect on the cerebellar mechanism for co-ordination and automatic equilibration.

I suggest, therefore, that there are three ways in which we can most conveniently approach this subject, viz : that we should first see what is the effect of alcohol in small quantities upon the process of thought, as for example in the correct perception of some object and the consequent reasoning thereupon ; secondly, its effect upon the actual performance of a voluntary movement; and thirdly, its effect on the cerebellum which has this co-ordinating influence on the great brain.

The Association Fibres of the Brain.

First as regards ideation, perhaps I had better give you a diagram illustrating the association fibres of the brain, which enable the perceptive and associating centres to work as a whole.

Within the last ten years it has been shown that the association fibres connect the different parts of the brain together, and must be in a state of activity during the process of ideation.   In fact, the whole of our knowledge of the disturbance of speech in certain forms of disease tends to show that it is the interruption of this association of the fibres which as much as anything causes the loss of that particular faculty.

This (fig. 12) is a diagram of a vertical section of the brain, showing here the frontal or forehead part, here the occipital or visual part, and here the parietal or part for the centres of muscular movement.   This diagram, which is quite faithful, shows us that all these parts are connected together by fibres.   This section only presents a minute fraction of the fibres that exist.   Every single part of the brain is therefore closely associated with other parts, thus providing that thoughts arising from stimulation of special sense centres can transmit their orders to other centres charged with the duty of putting thought into action.

Under these circumstances it is clear that in order to investigate the action of alcohol on such a complex process as that which I have just described as employed in effective ideation, we ought to first get down to elementary facts, and for this purpose we should begin by giving the brain, unstimulated, some exceedingly simple task to perform, and then after giving it a dose of alcohol make it repeat the task.

The activity of the brain in performing this function can be estimated by either measuring the relative times it takes to do some small task allotted to it, under these two conditions respectively, or by estimating the amount of work done in a given time, employing long periods to avoid errors.   The work on this subject has been chiefly carried out by Professor Kraepelin, and what he has accomplished is so valuable that his name ought to be a household word among us.

There are two things that have to be found out in such a method as the one I have suggested.   First, we have to discover how fast the
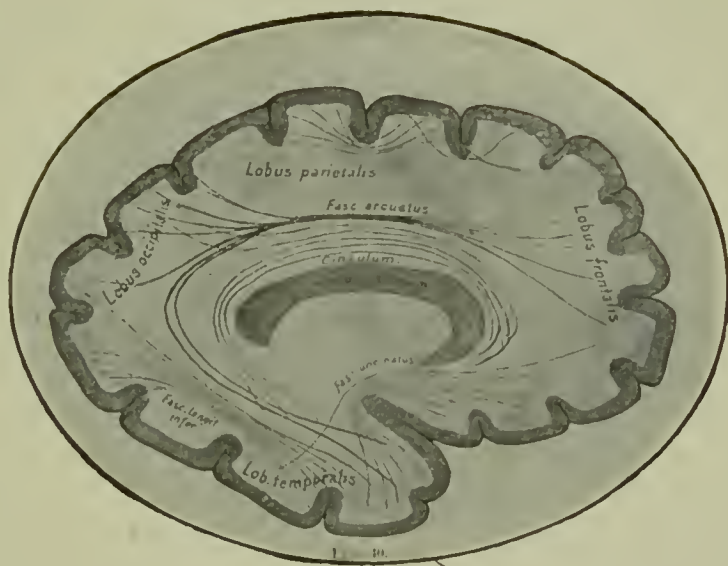
Fig. 12.

brain will work, and secondly, how accurately, for, as Professor Kraepelin has himself indicated, this latter factor is quite as important as the former, and the estimate, therefore, that we form of the effect of a substance like alcohol should be gauged as much by the quality of the work as by the speed with which it is accomplished.

Now, in order to attain this object we must have some means of exactly estimating the condition of the activity of the brain first working naturally, and then after alcohol.

The easiest way to do this is to measure what is called the reaction time. By the reaction time is meant that very small fraction of a second consumed by the nervous system in receiving an impression and executing some movement in answer to it, and infinitesimal though it be, in all minute and accurate records it is of vital importance. It is of such importance that astronomers have to measure their reaction period and to make allowance for it. The simplest way to explain how the measurement is taken is to demonstrate it in an experiment.

This shall be devised in order to estimate how quickly an observer, watching for the appearance of a given object, shall become conscious of the fact that it has appeared, *i.e.*, how quickly his brain has been able to take the idea in.

Simple Reaction Time Experiment.

Between the observer and myself we will place a rapidly revolving drum of blackened paper on which records can be made. I, from behind a screen, will suddenly display a small white flag (the object for which he is watching). In rising, the flag shall automatically cause, by opening a key, a small electrical signal to record the moment of its appearance by a mark on the blackened paper. Similarly, by pressing another key the observer shall also record on the paper the fact that he sees the flag. It follows, therefore, that if there be any space on the paper between the two marks, that space must indicate the delay between the appearance of the object and the observer's perception of it.

If, further, I apply to the blackened paper a tuning fork which vibrates at a very rapid rate, so that each half vibration is executed in $\frac{1}{500}$ of a second, I shall have upon the paper the interval between the two marks subscribed by a serrated line, each serrature indicating the fraction of a second which I have just mentioned. So I have only to add up the number of teeth in that interval to arrive at the exact fraction of a second consumed between the appearance of the flag and the observer's consciousness of it, and thus the required measurement is obtained.

We will now introduce a little complication. I will put upon the key another flag with a numeral upon it. I will ask the watcher to respond if the numeral consists of more than one unit, that is if it is 10 or above. If it is not above 9 I will ask him not to respond, in other words, I offer to him more thought, the necessity of thinking about

two things in place of one.   Under those circumstances you find that the interval of time is materially increased.   Of course, as before, the observer does not know the exact moment at which I am going to raise the figure.   (The lecturer then performed the experiment).

In the second experiment we find both from the sound interval between the clicking of the two keys and the space interval recorded on the drum, that the time employed in the complicated action was about a half more than in the simpler experiment.

That is a method of measuring the actual time that the nervous system as a whole takes to appreciate a sensation and to respond. But you will understand that that whole period of time, small though it be, includes not only the actual time occupied by the small cells of the brain during which they are compelled to operate, but it also includes the time spent in the passage of impulses from the eye to the brain and from the brain to the muscles.   Those intervals of time are known.

The period of transmission along a nerve fibre has been measured, so that we can exclude this by substraction, and in that way arrive at the true time spent by the cortical centres of the brain.   This method has been employed by numerous investigators, but by none with such complete accuracy as Professor Kraepelin, and he has thus been enabled to explain the contradictory and doubtful results arrived at by previous observers ; a most striking proof of the value of his researches.   Kraepelin found that the simple reaction period, the mere response to a signal, *i.e.*, as in the first experiment with the flag, was after the ingestion of a small quantity of alcohol, slightly accelerated, there was a slight shortening of the time, as though the brain were enabled to operate more quickly than before.   But he found that very speedily, after a few minutes, a slowing began, and became more marked and endured as long as the alcohol was in active operation in the body.   The time interval varied according to the individuals upon whom the experiments were performed.

Depressive Effect of Dietetic Quantities of Alcohol on the Highest Centres.

But he also found that the time occupied by a so-called complex reaction, a reaction in which there was an association of ideas, was never quickened by alcohol, that the slowing effect of the alcohol began from the first and continued throughout.   So that on the whole there is, even with the small quantities of alcohol which are called dietetic a distinct depressing effect upon the highest centres of the brain.

Another very striking result of his investigations was that they enabled him and other workers in his laboratory to demonstrate the absolute scientific truth of the picturesque saying that " Wine is a mocker."

Subjective Sensations of Increased Efficiency under Alcohol shown to be Mistaken.

In the investigation of complex reaction periods, involving greater thought, it had seemed to him that a small quantity of alcohol had an accelerating effect on the activity of his mind, that he performed the operations of adding and subtracting and learning figures more quickly. But when he came to measure on the drum the exact period of time, to his astonishment he found that he had accomplished these mental operations not more, but less, quickly than before, so that alcohol had a primarily deceptive influence on the mind, and its witness was a false witness.

This form of deception is not, of course, limited to alcohol, one of the common subjective sensations produced by extremely small doses of the ordinary anaesthetics used in surgery, *e.g.*, chloroform or ether, is that the patient possesses great muscular strength, and has a feeling of making powerful efforts which are not really in any way extraordinary and are readily controlled by the by-standers, the fact being that while the patient is entering the stage of unconsciousness the brain is being steadily paralysed.

From what I have said the truth of the very remarkable fact must be accepted, that when a person is in this stage of loss of cerebral activity after taking a small dose of alcohol, he feels that his brain is extraordinarily active. The idea is present to him that he is really thinking more than usual, whereas as a matter of fact his thinking is slower. That the subjective sensation of greater muscular power was a deception we have long known, it has been thoroughly established, but that the deception in regard to intellectual achievement was exactly parallel, even under the influence of very small doses of alcohol, this is new, and it proves to us that the sensation of well being usually associated with wine, beer, and spirits is only an illusion, and that once more when tried by the touchstone of experiment, "wine is a mocker."

Now this fact is of very great importance to us in endeavouring to understand how a substance which paralyses like alcohol can also stimulate. Alcohol is not peculiar in this respect; chloroform, or any of the drugs which we know send the brain to sleep have this property. Morphia, for instance, taken in very small quantity causes initial excitation. Can that be anything else than a paradox? In this respect these observations of the result of small quantities are most interesting to us from the physiological standpoint. They really offer the means whereby we can introspectively examine ourselves, and, as Professor Kraepelin has proved, our judgment—our intellectual judgment—is the first thing to fail. Our intellectual judgment must be associated with the very highest part of the ideation mechanism and its early failure under the action of alcohol is in harmony with the view that its operation should be referred to the smaller cells of the brain, as we learn from medical evidence that they are precisely the

ones which first succumb to the onset of disease   It is, therefore, now established that the first effect of alcohol in small quantities is to suspend or interfere with the operation of the highest function of the brain.

Alcohol Abrogates the Controlling Mechanism of the Brain.

Translated into popular language, it is as though a kind of brake were taken off, allowing the apparatus to go on more quickly than before, but with a higher and continuously increasing proportion of errors.   Thus it is clear that the first stimulation effect of alcohol, although apparently a help, is not a real help, for it abrogates that highest function we know in the brain, its controlling mechanism.

I now give you an example of this effect obtained by another agent which also stimulates first and then paralyses.   I refer to laughing gas.   Some fifteen years ago I made for another purpose a number of observations on myself as to the effect of laughing gas on the central nervous system.   In doing this it occurred to me that I could at the same time obtain evidence of how consciousness is lost under anaesthesia.   I arranged a table by my side with writing paper on it, held a pencil while the gas was administered to me, and resolved that I would write the figure 3, as being a simple mechanical act, in alternate rows.   This (fig. 13) is a photograph of the paper on which I began writing and at the same time inhaling the gas.   In fifty-five seconds I became unconscious, and concurrently you see the gradual decrease in the size of the figures, a phenomenon which is the representation in another form of that observed by patients when gradually becoming unconscious from fainting or from an epileptic attack—namely, the apparent diminution of size of objects they are looking at.   This effect is a feature of all forms of loss of conciousness.   You will see that, though the figures are written smaller, the more complicated thought is preserved and the writing of the threes in rows has not been disturbed.

I had arranged that during the period of unconsciousness a bystander should constantly urge me to write again, and, therefore, in obedience ultimately to his order, as soon as I began to recover consciousness I recommenced writing.   I remembered, as you see by the photograph, that I was to write threes, but although they are written correctly enough, they are no longer in alternate order—that is to say, the idea had been entirely blotted out of my mind by the very slight and fleeting poisoning of the cortical centres by the laughing gas.   It is remarkable how easily the cortex of the brain can by a little chemical intervention have blotted out from it the highest impressions—viz., those of ideation, and hence it is not surprising that we find that alcohol in those very small quantities which come within the so-called limit of the dietetic use of the drug first causes an apparent stimulation of the cortex, which is really loss of balance, and then very quickly paralyses its activity.
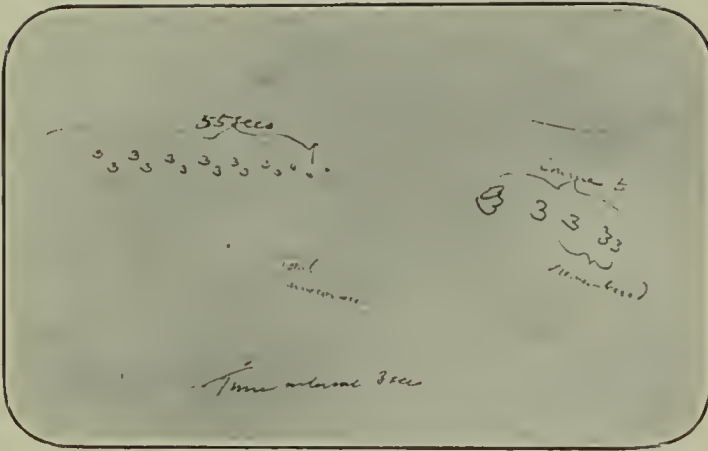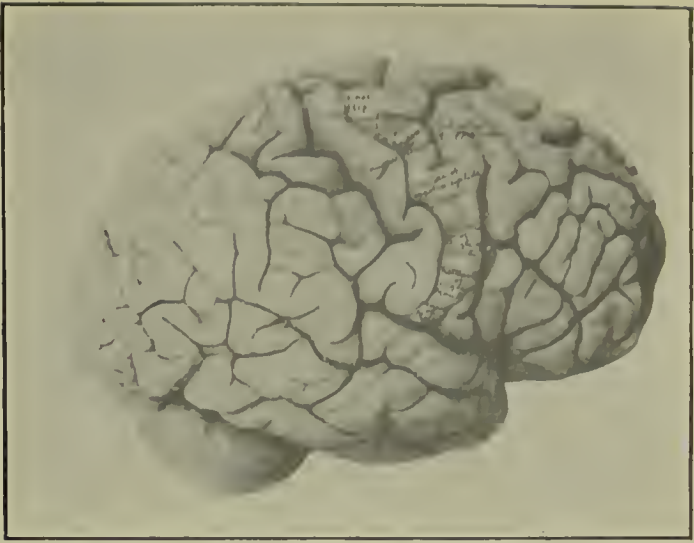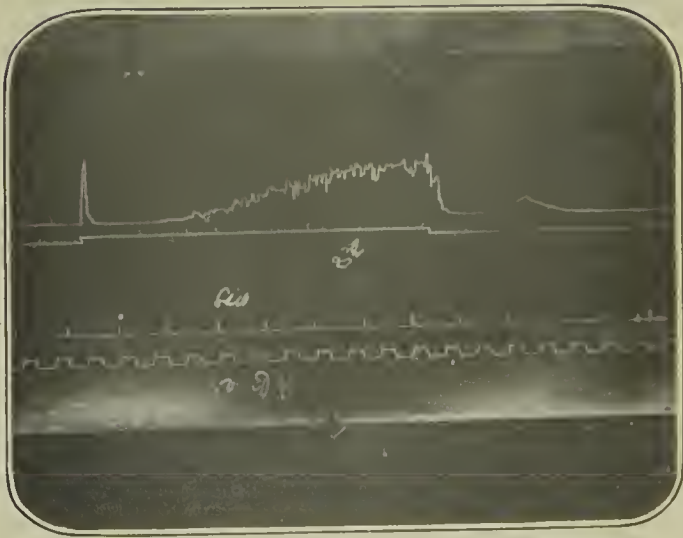
Fig. 13.

Fig. 14.

Fig. 15.

Passing now from the effects of the highest intellectual operations in the brain, I come to those acts of our conscious life which are half-way between the highly intellectual operation and the low automatism which the spinal cord is capable of carrying out, even when separated from the brain ; I refer to those purposeful acts which are frequently called voluntary acts, and which are spoken of by the early meta-physicians as " will," or " the volition power." Thanks to the work of Hitzig and Fritsch, in 1870, and especially of Ferrier, and to the investigations of numerous other physiologists the topography of the regions of the brain of animals, monkeys, dogs, cats, etc., in which are placed the centres for voluntary movements of the body has been finally determined.

In the monkey these situations have been mapped out accurately by experiment ; but in man, in certain operations for relief of epilepsy, it occasionally occurs that the brain has to be stimulated in order to find out exactly the spot that is to be removed, and in the course of operations of this kind facts have been acquired which I have put together, photographed, and propose now to discuss.

In the human brain these spots or motor centres on the convolutions are indicated on the photograph in writing (fig. 14). They are small portions of the cortex whence the movements start, and are called the centres for movement. Here is the centre for winking, the spot from which the nerve impulse starts. The movements of the thumb start from here, that being the part of the brain which gives out the order.

The nervous energy that produces a single contraction of a muscle is manifested in a kind of intermittent manner. It is not one impulse, it is a succession of impulses, and by means of suitable apparatus it can be demonstrated that such is the case. For instance, I have a small drum here air tight and fitted with an india-rubber end. If I press upon that india-rubber end, I shall produce a bulging in another india-rubber bag connected with it. A drum revolving by clockwork enables me to discover by means of the record on the smoked surface the exact rhythm at which my muscles contract if I make one volun-tary act of that kind (fig. 15). I will show it you by this lever, which I will try to raise slowly and with a uniform motion. I rest my whole hand on this bar and I cause one muscle, the long muscle which bends in the thumb, to pull against a strong spring and thereby raise the lever. You will at once see that I cannot do this smoothly and regularly, and that the action is not a continuous one, but one of successive steps. If I do it quickly I give it a swing, and it goes beyond the point I desire.

Now, from what I have already said, it is evident that the action I have just performed has emanated from the motor cortex of the brain, the region from whence impulses proceed to the muscles, and where, in fact, are placed the last out-going stations from which the messages pass, almost without a break, down along the white fibres in the brain and spinal marrow and along the nerves to the muscles.

In this connection it is interesting to note the cortical origin of the disease called epilepsy (which we now know to be in the main a want of control in these higher cortical centres) and, as Magnard points out, the dissolution of nerve tissue in the brain which alcohol produces, as well as the frequency with which it is found to be the cause of that disease.

Further, before the part of the cortical centre, which gives rise to the motor impulse in the muscles is paralysed by alcohol, the sensory part is already affected, and the subjective sensation of numbness or " pins and needles " referred to the tactile sense organs of the skin is experienced. This again is the same sensation as that felt by patients suffering from epilepsy due to mischief in the cortical centres of the brain, and harmonises completely with the observation of Magnard to which I have just referred.

There is yet another question in which the effect of alcohol, more especially on this part of the central nervous system, is of very great importance to us—namely, the question of fatigue, for it has been shown by Mosso, Waller, and others that the physiology of muscular fatigue is not a question so much of fatigue of the muscles (it certainly is not a question of fatigue of the nerve fibres leading from the nerve centres to the muscles) as of fatigue of the nerve centres in the so-called motor portion of the brain.

We have seen by my demonstration that we can very readily estimate the effect of a poison like alcohol on this part of the brain, for all we have to do is to select some voluntary muscular act and measure the amount of force which is evolved under normal circumstances by the sensori-motor cortex as exhibited by the contraction of the muscles, and compare it with the same force after the administration of alcohol.

Kraepelin's Experiment on Fatigue and Alcohol.

The simplest experiment of the kind is one such as described by Kraepelin, in which he measured on himself and a colleague, Dr. Dehio, the force with which they could grasp the dynamometer at regular intervals during the hour or more that the experiment lasted.

Even moderate doses of alcohol will produce tremor in all muscular acts. Kraepelin found that if he took a dynamometer—that is a little instrument which we can squeeze and which will record the amount of squeezing on a dial—and if he squeezed it at regular intervals for a certain time, while taking the records both before and after the effect of a small quantity of alcohol, he could accurately ascertain the amount of work put out, actuated as we know by these cortical centres in the brain. The results showed that there was at first an additional amount of work put out—an acceleration or stimulation, but that that was quickly followed again by the usual lowering or depressant effect.

The Effects of Alcohol and of Tea on Fatigue Contrasted.

Further, he found that if the person experimented upon had received, not a dose of alchohol, but a dose of tea, there was no lowering effect during the experiment beyond, of course, the ultimate effect of normal fatigue which has to be discounted in every experiment. The contrast, therefore, between alcohol and tea was most clearly marked in this matter of volitionary movement.

Two other workers, Messrs De Sarlos and Bernardinis, confirmed this discovery, and further showed that coffee caused also an increase in the reflex activity of the centres in the spinal cord. Experiments with tea thus show that there is an acceleration at first, the muscle contracting more quickly, and that there is an improvement in the force ; but there is no after paralysing effect when the stimulation stage has passed—in fact, there is no loss of power at all. This singularly strong argument in favour of total abstinence I am surprised to see has never found its way into Temperance literature. There is no question about the accuracy of the facts, and they have not been obtained merely by Kraepelin; but, as pointed out already, by other observers working on quite a different line.

It would be of interest if we could explain thoroughly the reason of the apparent acceleration of the output of work as the immediate effect of alcohol for the first few minutes. It is not possible for us to speak positively upon this point at the present time, yet from the records of the effect upon the tremor, the natural rhythm of the output of impulses, it undoubtedly must have to do with the loss of control. I mean that all our acts are under a certain brake power, like the governor of an engine. There are various drugs, such as alcohol, chloroform, ether, and others which have the power, which is no advantage to us, of taking away that controlling force. Kraepelin points out that whereas this acceleration can be frequently observed in the simple reaction experiments and also in the experiments on the volitionary motor centres of the brain, it is not found in the complicated thought measuring experiments. In these latter only the hampering influence is shown. There is an apparent temporary increase of activity, but it is an activity of the same kind as the " racing " of an engine when the governor is removed. This loss of control is, therefore, another evidence that these drugs act in a paralysing way from the beginning to the end of the experiment. This position is no new one. It has no doubt often been expressed on this very platform ; it was conceived years ago by Atkin and other observers and theorists in this country, on the question of alcohol. It has been the consistent teaching of the greatest physiological chemist that we know on the Continent, namely, Professor Bunge, and it cannot be insisted upon too strongly and too often that the apparent acceleration of the amount of work done is not a real thing ; it is, in fact, an evidence of the paralysing and deleterious effect of alcohol.

Compositors' Work with and without Alcohol.

I now desire to put before you a very careful series of observations made by Dr. Aschaffenberg on the dietetic use of alcohol in connection with skilled volitionary work.

It occurred to Dr. Aschaffenberg to choose for his experiments the work of compositors who at his suggestion offered themselves for the research. They were all skilled artisans, three of them accustomed to drink small quantities of alcohol, and a fourth who occasionally drank to excess.

Small intervals of time were taken and the total number of letters composed was first observed under circumstances of normal conditions, from which the necessary averages and observations of fatigue effects were obtained.

The nature of the result is shown very clearly in the accompanying table (fig. 16), which gives the relative figures for the number of letters set up in the second, third, fourth, and fifth quarters of an hour after the commencement of the experiments. The maximal difference and chief inhibitory action of the alcohol is well shown during the second quarter of an hour and remains obvious until towards the end of the experiment, when the effects were passing off. The dotted columns in the table represent the number of letters composed by the compositor after he had a small quantity of alcohol, and the plain part shows what the same man did without its intervention, and you will see that the results obtained are in complete harmony with those already given.

The next subject for our consideration in this matter is the influence of the cerebellum or small brain.

Although the cerebellum has been described for just as long a time as the large brain, we are still very much in the dark as to their relation with one another, but we know that if we wish to make any movement requiring fine adjustment of our limbs the cerebellum must act as well as the large brain or cerebrum.

It follows, therefore, that the cerebellum is intimately connected with the large brain and further it is known that injury to it results in loss of regulation and of control of movements. This is especially true of the muscles of the lower limbs. The legs are most particularly associated with the cerebellum, and standing and walking correctly in a co-ordinated fashion depend on its normal action. The nerve corpuscles which make up the larger structural elements of the cerebellum and give to it its characteristic appearance, and doubtless some of its functions, are known after their discoverer as Purkinje cells (fig. 17).

Alcohol especially Poisonous to the Cerebellum.

One of the further effects of alcohol in slightly larger doses than those we have been discussing is to destroy this special function of the cerebellum, and to produce a sensation of tremor and weakness in the lower limbs, so that the individual staggers slightly and finds standing
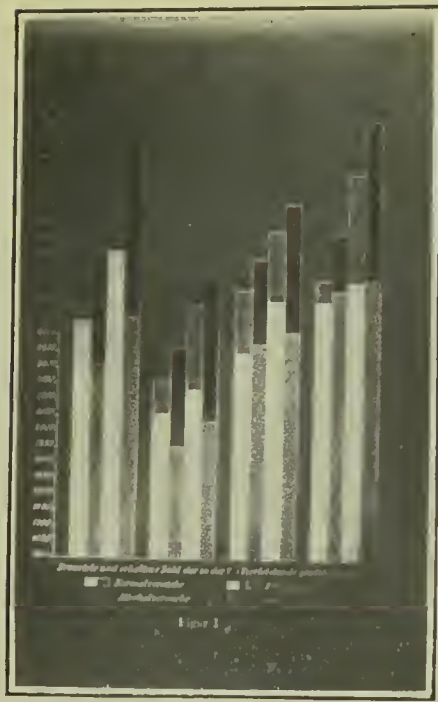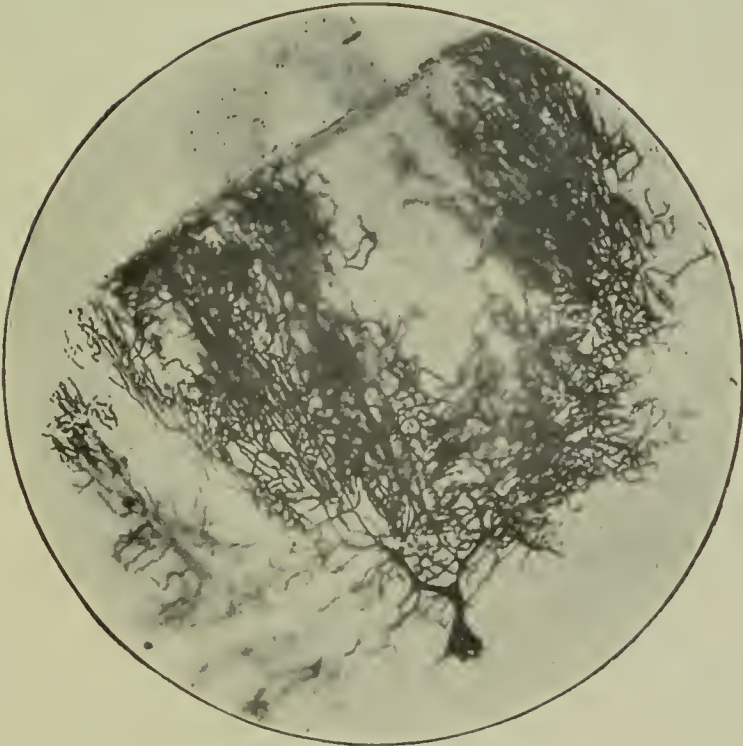
Fig. 16.

Fig. 17.

to be a matter of difficulty. Anyone who has observed slight alcoholic poisoning and compared it with the disordered equilibrium of a certain degree of disease of the cerebellum cannot fail to note the close similarity of the two conditions, or hesitate to accept the view that alcohol is particularly poisonous to the small brain or cerebellum.

Also we know from recent researches of Dr. Risien Russell that the cerebellum may have the function under normal circumstances of damping that tremor which we have seen is characteristic of the discharge of energy from a nerve cell. Hence in alcoholic poisoning that exaggeration of the natural intermittent discharge of the nerve centre which shows itself as a tremor may be due in part to the loss of cerebellar controlling influence as well as to the disturbance of the cortical cerebral apparatus.

There is a further phenomenon of a physiological kind which is an excellent illustration of the gradual disorganisation of the brain centres that alcohol produces, as it shows how that which is a perfectly normal way for a nerve centre to discharge becomes under some degenerating influence like that of alcohol, an affliction.

I have already shown that though a simple muscular movement might be supposed to consist of a single shortening of the muscle, this is not the case. A nerve centre does not send out one single gush of energy but a rapid intermittent stream of impulses. This was first discovered by two French investigators, Franc and Pitre, and since their original observations other experimenters have found that cortical voluntary centres pour out a succession of shocks, as it were, to the muscle at the rate of about twelve per second. In man we can obtain the same general result by voluntarily contracting the thumb in precisely the same manner and recording it in the same way as I have demonstrated. You will now readily understand that if the nerve centre is becoming disorganised this intermittent action will be exaggerated into a shock or tremor; hence it is of great interest, in studying the demoralization which alcohol produces on the brain, to know that this tremulousness, in the performance of a voluntary act, is an early and characteristic symptom, and the explanation of its occurrence is obvious.

We have now viewed the circumstances under which alcohol affects the nerve centres in the cortex of the brain, and in the cortex or grey substance of the cerebellum, but although our experimental methods have often involved record of the passage of the nerve impulses from the brain down the spinal cord and along the nerve fibres to the muscle, and depend for their record on the contraction of a muscle, I have from lack of time said nothing to you of the effect of alcohol on the spinal cord alone or on the nerves or on the muscles. I may tell you, however, that it is certain that the centres in the spinal cord, although they are undoubtedly in communication with the nerve fibres which come down from the brain, and thus form stations between the brain and muscles, do not appear to alter qualitatively

the character of the discharge of the nerve impulses from the cortex. Again, the nerve fibres running from such centres to the muscles become stimulated by alcohol when they are first exposed to its vapour, but are paralysed by prolonged exposure. This only adds to and does not in any way alter the conclusions I have stated to you. The observations of Waller, Mommsen and other physiologists on the peripheral nerves of the limbs, though extremely interesting and of great clinical importance, do not immediately affect my present subject.

In addition to the careful experimental results which I have put before you, the generally disadvantageous effects of alcohol on persons who do voluntary muscular work are exceedingly well-known, and it has of course been shown times out of number by athletic exhibitions, and by the records of travels and military expeditions, that the best physical results are obtained under total abstinence from the use of it even in such quantity as constitutes only a so-called article of diet.

Therefore the conclusion is overwhelming that even in very small quantities alcohol is injurious to the volitionary centres.

That leads me to come back now to the question whether these effects of alcohol in small quantities are really exerted on those corpuscles I showed you on the screen or not, and it will probably occur to you that one method of ascertaining this point would be to demonstrate under the microscope the structural changes which the alcohol would probably cause in them. The ingestion, however, of small quantities of alcohol produces no demonstrable changes in the structure of the nerve corpuscles ; in fact, it is not certain that the nerve corpuscles are the only parts of the nerve centre which do the work. We know they take a large part in it but it is possible they are not the only structures. The chemical processes of the body are so complex that it requires extremely little to upset the balance. In the case of people who suffer from gout, certain individuals will tell you perfectly truly that if they take a small quantity of a particular kind of alcoholic drink, champagne for example, it will invariably produce an attack, whereas they can take another kind of alcohol with apparent impunity. This shows, of course, that the chemical processes in their bodies may be upset by an astonishingly small quantity of the chemical reagent, and the effect, therefore, of so small a quantity of alcohol as suffices to influence the rapidity with which the nerve corpuscle is able to subserve the process of thought, could not possibly be expected to be demonstrable by any appreciable structural alteration.

Since, therefore, the chemical processes in the body are so delicate that an infinitesimal dose of poison (snake poison, for instance) can fatally arrest them without causing any changes of structure in the corpuscles which even the highest microscopical magnification can detect, we can certainly not expect to find such changes of structure in cases where the only evidence of disturbance of function is a slight
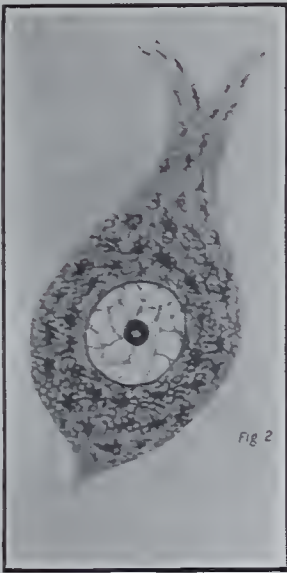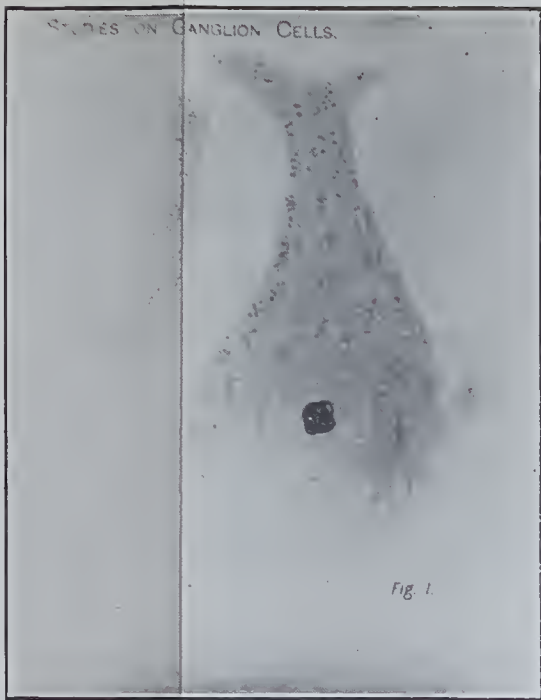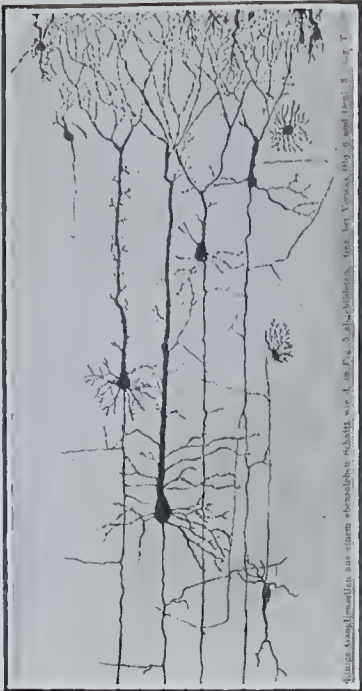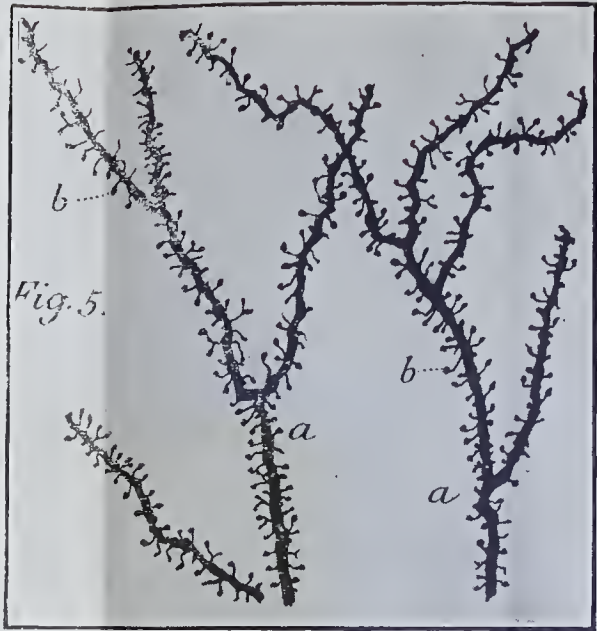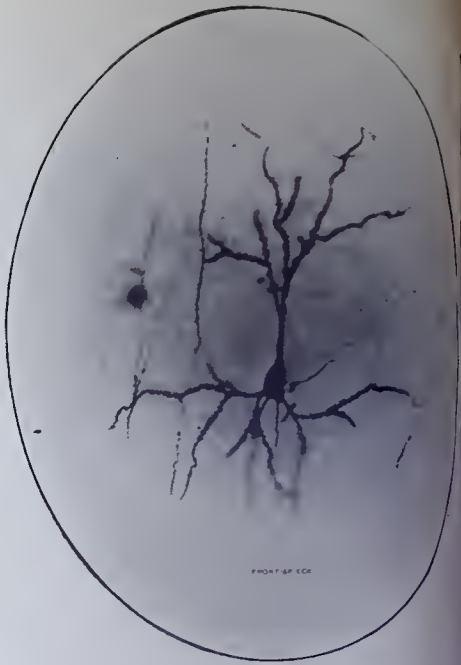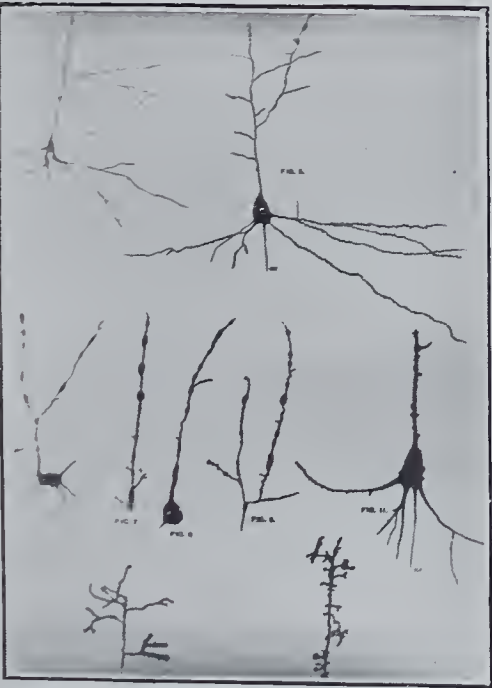
Fig. 18.

Fig. 19.

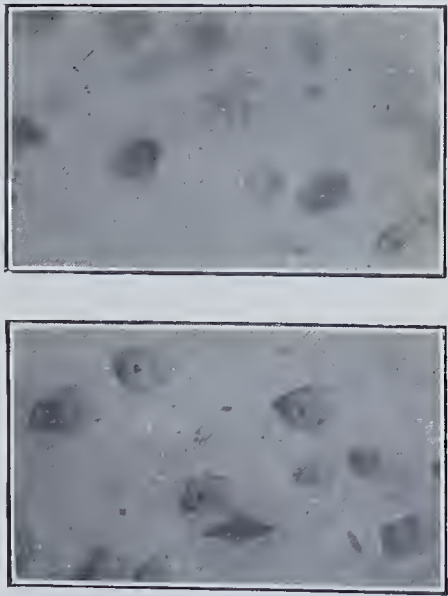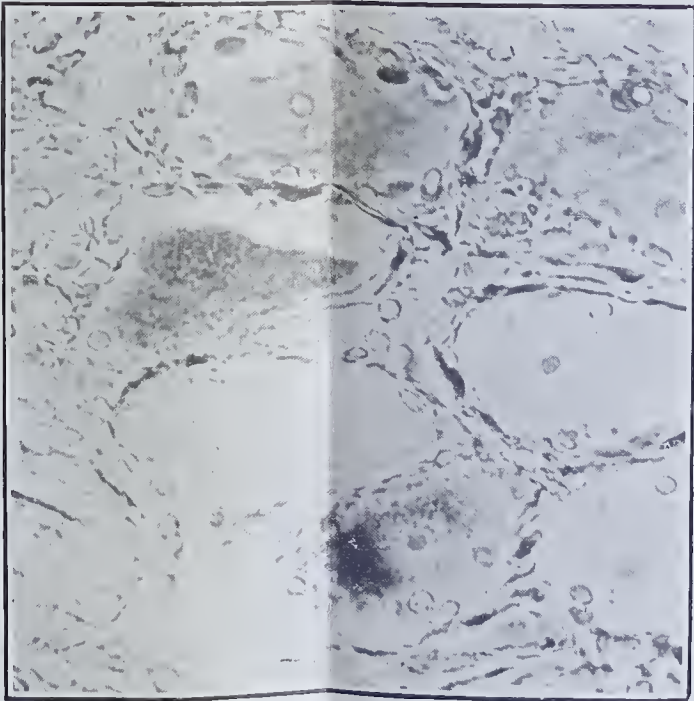Fig. 20

Fig. 21.

Fig. 22.

Fig. 23.

Fig. 24.

Fig. 25.

Fig. 26.

returdation in the ability to perform their task of the nerve corpuscles subserving the process of thought.

The researches of experimental physiology during the last twenty years into the functions of the brain have now completed in a logical manner our knowledge and analysis of the effect of alcohol on those of its centres which form the material basis or machinery for intellectual ideas.

The Structural Changes in the Brain in Prolonged Alcoholism.

The outward effects, the confusion of thought passing into stupor and unconsciousness, are too well-known to require description, but the structural changes which occur in the corpuscles of the brain in prolonged alcoholism must also be studied.

I spoke just now, for instance, of the Purkinje (fig. 17) nerve corpuscles, which constitute the chief nerve cell elements in the cerebellum or small brain. These nerve corpuscles, which have this wonderful arrangement of branches, bringing them into association with all the other structures in the cerebellum, exhibit under healthy conditions a nucleus and smaller granular masses in their protoplasm (fig. 18), but under the influence of alcohol the granular masses disappear (fig. 19), the protoplasm of the body of the corpuscle loses its characteristic structure and becomes a confused mass, and the nucleus is very greatly altered and distorted in shape.

The nerve cells, again, of the great brain, like Purkinje's corpuscles, have an extraordinary development of correlating branches (fig. 20). These, under normal conditions, have an even outline and innumerable little lateral twigs (figs. 21 and 22). Under the toxic influence of chronic alcoholism these branches exhibit swellings and shrinkings in their course (fig. 23) as well as similar alterations in the body of the wall of those observed in the cerebellum.

Finally, a remarkably constant feature of degeneration in the alcoholic person's brain is widespread pigmentation (fig. 24) in the nerve cells. The presence of pigment in the nerve cells in the human brain is a normal fact and occurs in animals, but in alcoholic poisoning this becomes exaggerated (fig. 25) at the same time that the protoplasm of the cell shrinks, so that ultimately the nerve corpuscle is represented by a shrivelled mass of pigment. In the early stages, as shown by this photograph from the periodical edited by Dr. Mott on the Diseases of the Brain, published under the auspices of the London County Council, the effect on the protoplasm of the bodies of the nerve cells is a degeneration producing clear bladder-like spaces or vacuoles (fig. 26), as they are termed.

In the face of structural alterations such as these the tremulousness and paralysis which are the final effects on the brain of the poison of alcohol need no further explanation ; or, to be precise, I must once more remind you that these last named changes in the structure are

only observed in the extreme cases, and to urge upon you that the practical argument for total abstinence is based on the irrefutable proofs derived from physiological investigation in contradistinction to anatomical and structural change.

One prominent defect in the study of the alcohol question has always been the want of really scientific proof that small quantities of alcohol as are used every day in ordinary diet have any appreciable adverse effect upon our organism. That defect has now been supplied. We have it definitely established by the precise and more delicate investigations and methods of the last ten or fifteen years that this is indeed the case.

From a scientific standpoint, therefore, the contention which we have so often had put before us by our friends, that small doses of alcohol, such as people take at meals, have practically no deleterious effect, cannot be maintained.

I have only touched upon a very small part of the subject, but if we consider the mass of work that has been accumulated from the observation of Parkes on physical work, from the observations of Ridge as to the stunting effects of small, extremely small, doses on the growth of vegetable protoplasm, and from the observations of Abbott and others on the weakening influence of alcohol on the structure of an animal when it is endeavouring to resist invasion by microbes (observations which show that alcohol, so far from improving the resistance of the body against disease-producing microbes, accelerates the destructive action of these enemies of the animal kingdom) we can only come to one conclusion, that from a scientific standpoint total abstinence must be our course if we are to follow the plain teaching of truth and common sense.

That even dietetic quantities of alcohol produce change in the nervous system is established on corroborative evidence, not, I think, to be disputed. That the change is a harmful one is equally clear. It is the part of the scientist, I think, to demonstrate this; but it is the part of the politician to persuade the nation to accept it, and to act upon it accordingly.
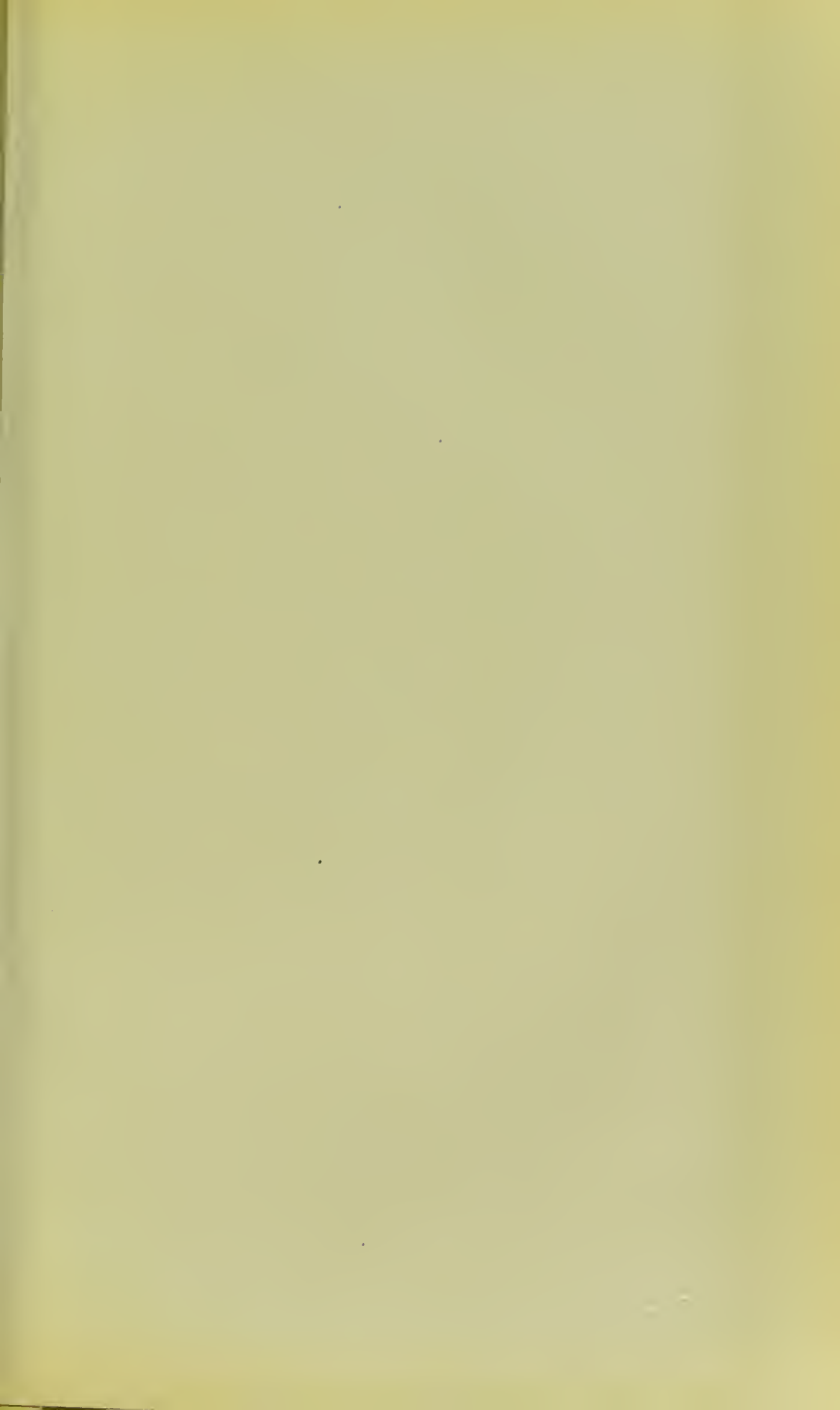
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